



NOVTRAN cDNA sequence:

atgcagtggctcgtctggcctgtaccctcctcagggctctccacatgtcctgtctcctgagagaccctgtgctgtgccacagggaccaagctcttc
cactcctgtatcacctcaacgaacccatgcgcctccttctggaggttgtgttgaagctgcaggcatccccctggactgtagggtctgagcaccgcc
ctgtccatccatccctgcatgctctcgttcacccgactccttcaacagaccatccccctgctcctctcaacagggcccgtctgtggggaacca
cggacagaggccttcccatcccaggcctgaaggccagagtaggtgggaccatcctcgccgaagccggcctcaattctcaaggccatgccgtggagc
cagtgcctctggaccctctgggtcaagcaaagggtgtgtctaatcaaaggcaggccctcgaggatgccaaaggccgcgaatgccagtggaccg
tgaaaaccttctgctgacaaacctgcagtgccttctctgctccagctgctctccagctctccatgcatcaaggtggaaacagagcaggagcgcagtatg
cggaaattgacttgcaaaagtccggccgctcgggattacaattcaagctgctgctgaaactcgggcagatcccagctgcaaaaggcagttccttctcga
gctgcagaacgtgtctggaggggttggtcagcccgaggtcccaggaaccactgcaaggtggggcgggccctcagagcccttcccagagctggg
ggctggtagcccccttggcttggagaaggctcagtacccaaccattcccaggcccgactgcggaagggtgtggactggccccctgtgtctcctggt
gaccagtgtccactgtgactctcccaggccagccgaacctggcacacactgggtgttccctaaatagccatggagggtattgtggcatggagagctgtc
gattccagaaacctcctggacatagggtcgggagctcatctgcagaagctgctga (SEQ ID NO: 1)

Fig. 1A

NOVTRAN Protein Sequence:

MQWSCLACTLLRVLPVLSLLRDPVPVPTGTKLFHSCITSTNPCASFLEVAVEAAGITPW
TVGSEHPPCPYPSLHASPFDTDFNRPSAPLNRPRSAGEPRTEAFPSPLKARVGGTILAE
AGLNSQGHAVEPVPSGSPSGSSKGCVLIKGRPSRMPKARECPVDRENLLLTPAVPSLLQL
LSSSPCIKVETEQERSNAEFDLQSRARDYNSRLLKLGQIPAAKGSSFLELQNVSGGVG
SARGPRNHCKVGAGPQSPFPELGAGSPPLALEKVSTQPIQARLRKGVDPVPSPGDQC
PLCTLPGQPNLAHTGCSLNSHGGYCGMESCRFQKPPGHRAGSSSAEAA (SEQ ID NO: 2)

Fig. 1B

09730617-070901



BlastN for NOVTRAN:
gb:GENBANK-ID:H55724|acc:H55724 CHR220663 Chromosome 22 exon Homo sapiens
genomic clone C22_916 5', mRNA sequence - Homo sapiens, 171 bp.

Minus Strand HSPs:

Score = 585 (87.8 bits), Expect = 1.0e-19, P = 1.0e-19
Identities = 117/117 (100%), Positives = 117/117 (100%), Strand = Minus /
Plus
Query: 735 ACCTCGGGCTGAGCCAACCCCTCCAGACAGTTCTGCAGCTCGAGGAAGGAACTGCCCTT 676
|||||
Sbjct: 18 ACCTCGGGCTGAGCCAACCCCTCCAGACAGTTCTGCAGCTCGAGGAAGGAACTGCCCTT 77

Query: 675 TGCAGCTGGGATCTGCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 619 (SEQ ID NO: 19)
|||||
Sbjct: 78 TGCAGCTGGGATCTGCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 134 (SEQ ID NO: 20)

Fig. 2A

09730617.070901



BlastX for NOVTRAN:

NoHits:

ptnr:SWISSPROT-ACC:P22357 ANHER-SPECIFIC PROTEIN SF18...	-3	102	0.0093	1
ptnr:SPTREMBL-ACC:Q26876 PROTECTIVE RECOMBINANT ANTIGE...	-3	87	0.018	1
ptnr:TREMBLNEW-ACC:AAD41775 PRO-ALPHA-2(I) COLLAGEN - ...	-3	86	0.061	2
ptnr:PIR-ID:S46272 anther-specific protein - common su...	-3	94	0.073	1
ptnr:SPTREMBL-ACC:Q26874 PROTECTIVE RECOMBINANT ANTIGE...	-3	78	0.16	1
ptnr:SPTREMBL-ACC:Q92029 ALPHA-1 COLLAGEN TYPE III - G...	-3	86	0.19	3
ptnr:SWISSPROT-ACC:P46804 SPIDROIN 2 (DRAGLINE SILK FI...	-3	101	0.24	1
ptnr:SPTREMBL-ACC:Q57808 103AA LONG HYPOTHETICAL PROTE...	+2	76	0.25	1
ptnr:SWISSNEW-ACC:P41484 PROLINE-RICH ANTIGEN (36 KD A...	-3	95	0.26	1

CuraBLASTX Analysis of AC007663_A

PUBLIC DATABASE

Query= AC007663 A Cura 109 transmembrane protein
(1047 letters) -

Database: /opt/database/public/blast/protnr
577,633 sequences; 178,813,065 total letters.

		Smallest		
			Sum	
Sequences producing High-scoring Segment Pairs:	Reading Frame	High Score	Probability P(N)	N
ptnr:SWISSPROT-ACC:P22357 ANHER-SPECIFIC PROTEIN SF18	-3	102	0.015	1
ptnr:pir-id:S12246 anther-specific protein SF18 precu	-3	102	0.015	1

PATENT DATABASE

CuraBLASTX Analysis of AC007663 A

Query= AC007663 A Cura 109 transmembrane protein
(1047 letters) of query sequence in all 6 reading frames

Database: /opt/database/licensed/blast/geneseq aa
349,121 sequences; 51,277,408 total letters.

		Smallest		
			Sum	
Sequences producing High-scoring Segment Pairs:	Reading Frame	High Score	Probability P(N)	N
patp:R28916 Type III procollagen (prior art) - Homo sa...	+1	81	0.059	3
patp:W03454 Mutant mouse c-AKT non-translation region ...	+1	81	0.075	1
patp:G04146 Arabidopsis thaliana protein fragment SEQ ...	-3	80	0.095	1

Fig. 2B

09730617-070901



NOVNEUR cDNA sequence:

Regions 135319 to 135129 (1-190bp) and 134487 to 134314 (191 to 364bp) of the genomic clone (in - frame). Further extended using ESTs AI739078, AI767488, and AI796217.

AGCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGCATGGCCCGCGCGGGAGGGCGCTCGGATGTTTCGGC
AGCCTCCTGCACTTCGCCCTGCTCGCTGCCGGCGTCCGCTCAGCTGGGATCTCCCGAGCCCCGCA
GCCGAGCCAGCAAGATCCGAGTGCACTCGCGAGGCAAGCTCTGGGCCATCGGTCACTTCATGGGCAAGAA
GAGTCTGGAGCCTTCCAGCCCATCCCCATTGGGGACAGCTCCCCACACCTCCCTGAGGGACCAGCGACTG
CAGCTGAGTCATGATCTGCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCG
CACCCCAAATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATGGGGCAGACA
CAACAGCGTGGCTTAGATTGTGCCCACCCAGGGAAGGTGCTGAATGGGACCCTGTTGATGGCCCCATCTG
GATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATTTCTGGCTGGGTCACCAGAAATATC
GCTGATGCAGACACAGATTATGTTCCCTGCTGTATTTCTGCTTCCCTGTTGAATTGGTGAATAAACCTT
GCTCTATACATAAAA (SEQ ID NO: 3)

Fig. 3A

NOVNEUR Protein sequence:

MFGSLLHFALLAAGVVPLSWDLPEPRSRASKIRVHSRGLWAIGHFMGKKSLEPSSPSPLGTAPHTSLRDQRLQLSH
DLLGILLKKALGVSLSRPAPQIQYRLLVQILQK (SEQ ID NO: 4)

Fig. 3B

05730617-070901



BlastN for NOVNEUR:

gb:GENBANK-ID:HUMNKB|acc:M21551 Human neuromedin B mRNA, complete cds -
Homo sapiens, 640 bp (RNA).

Top Previous Match Next Match
Length = 640

Plus Strand HSPs:

Score = 3055 (458.4 bits), Expect = 9.1e-132, P = 9.1e-132

Identities = 629/639 (98%), Positives = 629/639 (98%), Strand = Plus / Plus

Query 2 GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGC-ATGGCCCG-CGG-CGGGAGGGCGCT 58
GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGC ATGGCCCG CGG CGGG GGGCGCT
Sbjct: 2 GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGCCATGGCCCGCGGGCGGG-GGGCGCT 60

Query: 59 CGGATGTTCCGCGAGCCTCCTGCACCTTCGCCCTGCTCGCTGCCCGGCTCGTCCGCTCAGC 118
CGGATGTTCCGCGAGCCTCCTGC CTTGCCCTGCTCGCTGCCCGGCTCG CCGCTCAGC
Sbjct: 61 CGGATGTTCCGCGAGCCTCCTGCTCTTCGCCCTGCTCGCTGCCCGGCTCGCCCCGCTCAGC 120

Query: 119 TGGGATCTCCCGGAGCCCCGAGCCGAGCCAGCAAGATCCGAGTGCACTCGCGAGGCAAG 178
TGGGATCTCCCGGAGCCCCGAGCCGAGCCAGCAAGATCCGAGTGCACTCGCGAGGCAA
Sbjct: 121 TGGGATCTCCCGGAGCCCCGAGCCGAGCCAGCAAGATCCGAGTGCACTCGCGAGGCAAC 180

Query: 179 CTCCTGGGCCATCGGTCACTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCCCA 238
CTCCTGGGCCA CGGTCACTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCC A
Sbjct: 181 CTCCTGGGCCACCGGTCACTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCC-A 239

Query: 239 TTGGGGACAGCTCCCCACACCTCCC-TGAGGGACAGCGACTGCAGCTGAGTCATGATCT 297
TTGGGGACAGCTCCCCACACCTCCC TGAGGGACAGCGACTGCAGCTGAGTCATGATCT
Sbjct: 240 TTGGGGACAGCTCCCCACACCTCCCCTGAGGGACAGCGACTGCAGCTGAGTCATGATCT 299

Query: 298 GCTCGGAATCCTCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCGCACCCCCA 357
GCTCGGAATCCTCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCGCACCCCCA
Sbjct: 300 GCTCGGAATCCTCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCGCACCCCCA 359

Query: 358 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT-GGGGCA 416
AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT GGGGCA
Sbjct: 360 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATAGGGGCA 419

Query: 417 GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCCTGTT 476
GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCCTGTT
Sbjct: 420 GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCCTGTT 479

Query: 477 GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 536
GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT
Sbjct: 480 GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 539

Query: 537 TCTGGCTGGGTACCCAGAAATATCGCTGATGCAGACACAGATTATGTTCTGCTGTATTT 596
TCTGGCTGGGTACCCAGAAATATCGCTGATGCAGACACAGATTATGTTCTGCTGTATTT
Sbjct: 540 TCTGGCTGGGTACCCAGAAATATCGCTGATGCAGACACAGATTATGTTCTGCTGTATTT 599

Query: 597 CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCTAT 637 (SEQ ID NO: 21)
CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCT T (SEQ ID NO: 22)
Sbjct: 600 CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCTTT 640 (SEQ ID NO: 23)

Fig. 4A

05730517.070501



BlastX for NOVNEUR:
ptnr:SWISSPROT-ACC:P08949 NEUROMEDIN B-32 PRECURSOR [CONTAINS: NEUROMEDIN
B] - Homo sapiens (Human), 121 aa.

Top Previous Match Next Match
Length = 121

Plus Strand HSPs:

Score = 513 (180.6 bits), Expect = 1.9e-48, P = 1.9e-48
Identities = 105/118 (88%), Positives = 105/118 (88%), Frame = +2

Query: 44 RREGARMFGSLHFFALLAAGVPLSWDLPEPRSRASKIRVHSRGKLWAIGHFMGKKSLEP 223
R GARMFGSLL FALLAAGV PLSWDLPEPRSRASKIRVHSRG LWA GHFMGKKSLEP
Sbjct: 4 RAGGARMFGSLLL FALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKSLEP 63

Query: 224 SSPSPILGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIYRRLVQILQK 397 (SEQ ID NO: 24)
SSPS G P LRDQRLQLSHDLLGILLKKALGVSLSRPAPQIYRRLVQILQK (SEQ ID NO: 25)
Sbjct: 64 SSPSHWQQLPTPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIYRRLVQILQK 121 (SEQ ID NO: 26)

Fig. 4B

ClustalW for NOVNEUR:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g., L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) A37178 (neuromedin B precursor - rat): Locus A37178, accession A37178, PID - g1 12182
- 2) NEUB_HUMAN (NEUROMEDIN B-32 PRECURSOR): Locus - NEUB_HUMAN, accession - P08949, PID - g1346684

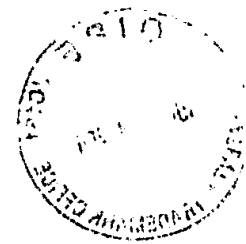
Neuromedin_New_REVCOMP -----MFGSLHFFALLAAGVPLSWDLPEPRSRASKIRVHSRGKLWAIGHFMGKKS
A37178 MTRQAGSTWLLRGLLLEFALFVSCITPEFSDWDLPEPRSRASKIRVHPRGNLWATGHFMGKKS
NEUB_HUMAN MARRAGGARMFGSLLL FALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS

Neuromedin_New_REVCOMP LEPSSPSPLGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIYRRLVQILQ
A37178 LEPSPSLVGTAPPTITQREORIQLSHDLLRILLQKALGMNLGSPAPPQIYRRLQK---
NEUB_HUMAN LEPSSPSHWQQLPTPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIYRRLVQILQ

Neuromedin_New_REVCOMP K (SEQ ID NO: 27)
A37178 - (SEQ ID NO: 28)
NEUB_HUMAN K (SEQ ID NO: 29)

Fig. 5

05730617-070501



NOVGON cDNA sequence:

1
ATGAAGCTGGCATTCCTCTTCCTTGGCCCCATGGCCCTCCTCCTTCTGGCTGGCTATGGCTGTGTCTCGGTGCCTCCAG
81
TGGGAACCTGGCACCCTTTGTGGGCTGTGCCGTGAGGGAGTTTACTTTCTGGCCAAGAAGCCAGGCTGCAGGGGCTTC
161
GGATCACCAAGGATGCCTGTGGGGTGGCTGTGAGACCTGGGAGAAACCAATTCGGAACCCCTATATTGAAGCCCAT
241
CATCGAGTCTGTACCTACAACGAGACCAAACAGGTGACTGTCAAGCTGCCCAACTGTGCCCCGGGAGTCGACCCCTTCTA
321
CACCTATCCCGTGGCCATCCGCTGTGACTGCGGAGCCTGCTCCACTGCCACCACGGAGCTGAGGTTGATGCCAGGGGAAG
401
CTGCTGTGGCACTGGGCTTCTGGTGTGAGCTAGGAGACAGGGATCTAGGACAACAGGGACCAGGTGGCGACATGCAGCT
481
GTAAGAGACAAGGTGAGTCTCCTGAAGGCAGTAGATGGTTGGAATGGGCTGCTTGGGGACCCAGCGAGCTCCAGGGCCT
561
TTCTGCTTCTTCTGTACCCCTGTATTTCCCTTGGCTTCCAAATTGACTCAGCTTCTGGTAAAGTTGGAAACTTTTCCA
641
GCAAACAGACCTTCATCTTCTCCAGTGCAGAGATTACATTAGGAGGAACATGA (SEQ ID NO: 5)

Fig. 6A

NOVGON Protein Sequence:

MKLAFLFLGPMALLLLAGYGCVLGASSGNLRTFVGCAVREFTFLAKKPGCRGLRITDA
CWGRCEIWEKPILEPPYIEAHRVCTYNETHQVTVKLPNCAGVDPFYTPVAIRCDCG
ACSTATTTELRLMPGEAAVALGFWCQRRRQGSRTTGTWRHAAVRDKVSLLKAVDGN
NGLLGDPASSQGLSASSCTPVFPLAFQIDSASGKVGNFSSKQTFIFSSAEITLGGT* (SEQ ID NO: 6)

Fig. 6B

09730617-070901



BlastN for NOVGON:

AF146151 *Salmo salar* gonadotropin II beta subunit mRNA,
partial cds - *Salmo salar*, 266 bp (RNA).

Top Previous Match Next Match
Length = 266

Plus Strand_HSPs:

Score = 208 (31.2 bits), Expect = 0.043, P = 0.042

Identities = 124/205 (60%), Positives = 124/205 (60%), Strand = Plus / Plus

Query: 177 CTGCTGGGGTGGCTGTGAGACCTGGGAGAAACCCATTCTGGAACCCCCCTATATGAAGC 236
CTGC G GG C CTG G ACC GGAG CC TT T AA CCC AT TT A C
Sbjct: 34 CTGCAGTGGCCACTGCGTCACCAAGGAG---CCGGTTTTC-AAGAGCCC-ATTTTCACC 88

Query: 237 CCAT-C-ATCGAGTCTGTACCTACAAAGA-GACCAAACAGGTGACTGTCAAGCTGCCCAA 293
T C A C GT TG ACCTAC GA G CC A G AC TC CT CC A
Sbjct: 89 GTGTACCAGCATGTGTGCACCTACCGGGACGTCGGCT-ATGAAACGATCCGCCTACCTGA 147

Query: 294 CTGTGCCCCGGGAGTCGACCC-CTTCTACACCTATCCCGTGGCCATCCGCTGTGACTGGC 352
CTGT CCCC G GT GACC C T T CACCTA CC GTGGC T GCTGTGACTGC
Sbjct: 148 CTGTCCCCCTTGGGTGGACCATCATGT-CACCTACCTGTGGCTCTGAGCTGTGACTGCA 206

Query: 353 GAGCCTGCTCCACTGCCACCACGGAGCTG 381 (SEQ ID NO: 30)
G CTG CA G CAC C GA CTG (SEQ ID NO: 31)
Sbjct: 207 GCCTCTGTAACATGGACATTCTGA-CTG 234 (SEQ ID NO: 32)

Fig. 7A

05730617.070501



BlastX for NOVGN:

P01235 GONADOTROPIN BETA CHAIN PRECURSOR - *Cyprinus carpio* (Common carp), 144 aa.

Score = 203 (71.5 bits), Expect = 2.3e-16, P = 2.3e-16

Identities = 37/85 (43%), Positives = 52/85 (61%)

Query: 42 TFLAKKPGC-RGLRITTDACWGRCEWKEPPIEPPYIEAHRVCTYNETKQVTVKLPNCA 100
T +K GC + L + T C G C T E P+ + P+ + VCTY + + TV+LP+C
Sbjct: 39 TVAVEKEGCPKCLVLQTTICSGHCLTKE-PVYKSPFSTVYQHVCTYRDVRYETVRLPDCP 97

Query: 101 PGVDPFYTPVAIRCDGACSTATTE 126 (SEQ ID NO: 33)

PGVDP TYPVA+ CDC C+ T++ (SEQ ID NO: 34)

Sbjct: 98 PGVDPHITYPVALSCDCSLCTMDTSD 123 (SEQ ID NO: 35)

>ptnr:SWISSNEW-ACC:Q9YGH2 GONADOTROPIN BETA-II CHAIN PRECURSOR (GTH-II-BETA)
- *Clupea pallasii* (Pacific herring), 149 aa.

Plus Strand HSPs:

Score = 206 (72.5 bits), Expect = 1.0e-15, P = 1.0e-15

Identities = 47/117 (40%), Positives = 63/117 (53%), Frame = +1

Query: 28 PMALLLAGYGCVLG--ASSGNLRTFVGCAVREFTFLAKKPGC-RGLRITTDACWGRCE 198
P +LL CVL A NL+ C+ T +K GC R L T C G C T
Sbjct: 5 PECTILLLLCMCVLAVPAQCFLQP---CVLVNETVSVEKEGCPRLVFRTTICSGHCPT 61

Query: 199 WEKPILEPPYIEAHRVCTYNETKQVTVKLPNCAPGVDPFYTPVAIRCDGACSTATTE 378 (SEQ ID NO: 36)

E P+ + P+ + VCTY + T++LP+CA GVDP TYPVA+ C+C CS T++ (SEQ ID NO: 37)

Sbjct: 62 KE-PVYKSPFSVVNHQVCTYGNFRYETIRLPDCADGVDPVLYTPVALSCDCSLCSMDTSD 120 (SEQ ID NO: 38)

>patp:R15106 hCG/bLH chimera, D10 - *Homo sapiens*, 145 aa.

Plus Strand HSPs:

Score = 188 (66.2 bits), Expect = 5.0e-14, P = 5.0e-14

Identities = 40/101 (39%), Positives = 58/101 (57%), Frame = +1

Query: 76 SSGNLRTFVGCAVREFTFLAKKPGCRG-LRITTDACWGRCEWKE--PILEPPYIEAHR 246
S G LR C T A+K C + TT C G C + ++ P++ PP + R
Sbjct: 1 SRGPLRPL--CQPINATLAAEKEACPVCITFTTICAGYCPMKRVLPVILPMPQ---R 55

Query: 247 VCTYNETKQVTVKLPNCAPGVDPFYTPVAIRCDGACSTATTE 378 (SEQ ID NO: 39)

VCTY+E + +V+LP C PGVDP ++PVA+ C CG C ++T+ (SEQ ID NO: 40)

Sbjct: 56 VCTYHELRFASVRLPGCPPGVDPMSFPVALSCHCGPCRLSSTD 99 (SEQ ID NO: 41)

>patp:W65110 Equine chorionic gonadotropin beta-chain protein - *Equus caballus*, 169 aa.

Plus Strand HSPs:

Score = 175 (61.6 bits), Expect = 1.2e-12, P = 1.2e-12

Identities = 43/116 (37%), Positives = 60/116 (51%), Frame = +1

Query: 31 MAILLLAGYGCVLGASSGNLRTFVGCAVREFTFLAKKPGCR-GLRITTDACWGRCEWKE 207
+ L +L G V AS G LR C T A+K C + TT C G C + +
Sbjct: 7 LLLWMLLSVGVW-ASRGPLRPL--CRPINATLAAEKEACPICITFTTICAGYCPMSVR 63

Query: 208 PILEPPYIEAHR-VCTYNETKQVTVKLPNCAPGVDPFYTPVAIRCDGACSTATTE 378 (SEQ ID NO: 42)

+ P + A + VCTY E + +++LP C PGVDP ++PVA+ C CG C TT+ (SEQ ID NO: 43)

Sbjct: 64 VM--PALPAIPQPVCTYRELRFASIRLPGCCPPGVDPMSFPVALSCHCGPCQIKTTD 119 (SEQ ID NO: 44)

Fig. 7B

05730617-070901



ClustalW alignment for NOVAGON:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

GTHB_CYPCA	MCTPVKLLVNRNHLFSVVLHAVAQSS---YLPPCEPVNETVAVEKEGCPKCLVLQTTI
Q98849_OTHB2_GOLDFISH	MCTPVKLLV---LFSVVLHAVAQSS---YLPPCEPVNETVAVEKEGCPKCLVLQTTI
LSHB_BOVIN	MEMFOCLLW---LLLGVAAGWASRGP---LRPLCOPINATLAAEKBACPVCTITFTSI
LSHB_SHEEP	MEMFOCLLW---LLLGVAAGWASRGP---LRPLCOPINATLAAEKBACPVCTITFTSI
novel_gonadotropin	MKEAFLFLGPMALLLLAGYGVLCASSGNLRTFVGCDAVREFTFLAKKPGCRG-LRIITDA

GTHB_CYPCA	CSGHCLT-KBPVYKSPSTWYCHVCTYRDVRYETVRLPDCPPGVDPHITYPVALSCDCSL
Q98849_GTHB2_GOLDFISH	CSGHCLT-KBPVYKSPSTWYCHVCTYRDVRYETVRLPDCPPGVDPHITYPVALSCDCSL
LSHB_BOVIN	CACYCPS-MKRVLPVILPPMPORVCTYHELRFAFVRLPCCPPGVDPMVSPVALSCHCGP
LSHB_SHEEP	CACYCPS-MKRVLPVILPPMPORVCTYHELRFAFVRLPCCPPGVDPMVSPVALSCHCGP
novel_gonadotropin	QWGRCTWEKPILEPPYIEAHHRVCTYNETKQVTVKLPNCAPGVDPFPYTPVAIRCDGGA

GTHB_CYPCA	CTMDTSD-----CT---IESLOPDFOMSQ-REDFLVY-----
Q98849_GTHB2_GOLDFISH	CTMDTSD-----CT---IESLOPDFOMSQ-REDFLVY-----
LSHB_BOVIN	CRISSTD-----CG---GPRTQPLACDHPPLPDILFT-----
LSHB_SHEEP	CRISSTD-----CG---GPRTQPLACDHPPLPDILFT-----
novel_gonadotropin	CSTATTELRLMPGEAAVALGFWCQRRROGSRITGTRWRHAAVRDKVSLKAVDGNWLLG

GTHB_CYPCA	----- (SEQ ID NO: 45)
Q98849_GTHB2_GOLDFISH	----- (SEQ ID NO: 46)
LSHB_BOVIN	----- (SEQ ID NO: 47)
LSHB_SHEEP	----- (SEQ ID NO: 48)
novel_gonadotropin	DPASSQGLSASSCTPVFPLAFQIDSASGKVGNFSSKQTFIFSSAEITLGGT (SEQ ID NO: 49)

Fig. 8

NOVINTRA A cDNA sequence:

Regions 116708 to 116812 (1-105bp), 117121 to 117248 (106-233p), and 117529 to 117778 (234-483bp).

CACTGTCATACTGTTTCAGAAATTAAATATGCAGACCAGAAGGCTCTATACACAAGAG
ATGGCCAGCTGCTGGTGGGAGATCCTGTGTCAGACAAGCTGTGTCAGAGAAGATC
TGCATACTTCTAACAGAGGCTTGGCCCGCACCAAGGTCCCCATTTTCTGGGGATC
CAGGGAGGGAGCCGCTGCCTGGCATGTGTGGAGACAGAAGAGGGGCCCTTCCTACA
GCTGGAGCCATCCACCTTGCCCCACAGATGTGAACATTGAGGAAGTGTACAAAG
GTGGTGAAGAGGCCACAGCTTCACTTCTCCAGAGCAGCTCAGGCTCCGCCCTTCA
GGCTTGAGGCTGCTGCTGGCTGGCTGGTTCCTGTGTGGCCCGGCAGAGCCCAGC
AGCCAGTACAGCTACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTTTACTTTG
AACAGAGCTGGTAGGAGACAGGAACTGC (SEQ ID NO: 7)

Fig. 9A

NOVINTRA A Protein sequence:

LSYCFRIKYADQKALYTRDQQLLVGDPVADNCCAEEKICILPNRGLARTKVPIFLGIQGGG
RCLACVETEBGSLQLEPSTLPPQDVNIEELYKGGEEATRTFFQSSSGSAFRLEAAAWP
GWFLCGPAEPQQPVQLTKESEPSARTKFYFEQSW (SEQ ID NO: 8)

Fig. 9B

09730617.070501



BlastN for NOVINTRA A:

gb:GENBANK-ID:AF072476|acc:AF072476 Equus caballus interleukin-1 receptor
antagonist secretory form (IL-lra) gene, partial cds - Equus caballus,
221
bp.

Top Previous Match Next Match

Length = 221

Plus Strand HSPs:

Score = 321 (48.2 bits), Expect = 8.1e-08, P = 8.1e-08

Identities = 147/218 (67%), Positives = 147/218 (67%), Strand = Plus / Plus

Query: 253 AGGATGTGAACATTGAGGAACGTACAA-AGGTGGTGAAGAGGCCACCGCTTCACCTTC 311

AGG GT AACAT GA CTG CAA A G GA GAG CA CGCTTCACCTTC

Sbjct: 4 AGGCAGTTAACATCACTGACCTGAGCAAGAACAAG-GAGGAGAACAAGCGCTTCACCTTC 62

Query: 312 TTCCAGAGCAG-CTCAGGCTCCGCCTTCAGGCTT-GAGGCTGCTGCCTGGCCTGGCTGGT 369

TCC G CA C GGC CC CC CAG CTT GAG CTGC GCCTG CCTGGCTGGT

Sbjct: 63 ATCC-GCTCAACAGTGGCCCCACCACCAG-CTTCGAGTCTGCCGCTGCCCTGGCTGGT 120

Query: 370 TCCTGTGTGGCCCGGCAG-AGCCCCAGCAGCCAGTACAGC-TCACCAAGGAG---AGTGA 424

TCCT TG CG CAG AG C A C GCC GT CAGC TCACCAA AG A GA

Sbjct: 121 TCCTCTGCACGGCG-CAGGAGGCAGACGGCCCGT-CAGCCTCACCAACAAGCCCAAAGA 178

Query: 425 GCCCT-CAGCCCGT-ACCAAGTTTACTTTGAACAGAGCTGGTAG 467 (SEQ ID NO: 50)

G CCT CA GT ACCAAGTT TACTT A AG C GTAG (SEQ ID NO: 51)

Sbjct: 179 GTCCTTCATG--GTCACCAAGTTCTACTTCCAGGAGGACCAAGTAG 221 (SEQ ID NO: 52)

Fig. 10A

09730617-070901



BlastX for NOVINTRA A:

ptnr:TREMBLNEW-ACC:CAB59831 IL-1L1 PROTEIN - Mus musculus (Mouse), 155 aa.

Top Previous Match Next Match

Length = 155

Plus Strand HSPs:

Score = 309 (108.8 bits), Expect = 8.0e-27, P = 8.0e-27

Identities = 70/149 (46%), Positives = 93/149 (62%), Frame = +3

Query: 12 CFRIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLARTKVPIFLGIQGGSRC 188

Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHAEKVIKGEIISVVPNRALDASLSPVILGVQGGSC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEATRFTFFQSSSGSAFRLEAAAWPGW 368

Sbjct: 68 LSC-GTEKGPILKLEP-----VNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQQPVQLTKESEPSAR----TKFYFEQ 458 (SEQ ID NO: 53)

Sbjct: 120 FLCTSPREADQPVRILTQIPEDPAWDAPITDFYFQQ 153 (SEQ ID NO: 55)

>ptnr:SPTREMBL-ACC:Q9UBH0 FIL1 DELTA (INTERLEUKIN-1 LIKE PROTEIN 1)
(INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG 1) (INTERLEUKIN-1 DELTA) - Homo
sapiens (Human), 155 aa.

Plus Strand HSPs:

Score = 285 (100.3 bits), Expect = 4.3e-24, P = 4.3e-24

Identities = 67/149 (44%), Positives = 89/149 (59%), Frame = +3

Query: 12 CFRIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLARTKVPIFLGIQGGSRC 188

Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHAGKVIKGEIISVVPNRWLDASLSPVILGVQGGSC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEATRFTFFQSSSGSAFRLEAAAWPGW 368

Sbjct: 68 LSCGVGQE-PTLTLEP-----VNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQQPVQLTKESEPSAR----TKFYFEQ 458 (SEQ ID NO: 56)

Sbjct: 120 FLCTVPEADQPVRILTQLPENGGWNAPITDFYFQQ 153 (SEQ ID NO: 58)

Fig. 10B

09730617-070901



ClustalW for NOVINTRA A:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) X86458spoil1 (cDNA encoding a human spoil-I protein); X86459spoil2 (cDNA encoding a human spoil-II protein); X89432-illdelta (human IL-1 delta encoding cDNA); Q14628 (intracellular IL-1 receptor antagonist type II-human); G512010illbeta (ovine Il-1 beta - pig)

```
X86458spoil1  -----DNHIMRGTPGDA-----DGG--GRAVYQS-----
X86459spoil2  -----DNHIMRGTPGDA-----DGG--GRAVYQSSESNAVGMLWRLRPSALTSPV
X89432-illdelta -----MALADLYEEG-----CGG--GGEEDNADSK-----E-----
Q14628
illbeta-1DNA
G512010illbeta MATVPEPINVWYYSDENELLFEVDGPKQMKSCTHLDLGSMGDGNIQLQISHQLYNKS

X86458spoil1  -----MCKPITGTINDLNQCVWILQGNLVAVPRSDS--VTPVTVAVIT
X86459spoil2  EAPAFSAPLCTLPFPVPCKPITGTINDLNQCVWILQGNLVAVPRSDS--VTPVTVAVIT
X89432-illdelta -----MVLSCALCFRMKDSALKVLYTHNNOLLACGLHA----GKVIKGEET
Q14628 -----TICRPSGRKSSKMQAFRIADNNOKTFYLRNNOLVAGYLOG----PNVNLEKI
illbeta-1DNA -----GPSALSYCFRIKYADOKALYTRDGOLLVGDPA----DNCCAEKI
G512010illbeta FRQVSVIVAMEKLRSRAYEHVFRDDDLRSILSFIFEEEPVIFETSSDELLCDAAVQSVK

X86458spoil1  CKYPEAL-----EGRGDPHYLGIONPEM
X86459spoil2  CKYPEAL-----EGRGDPHYLGIONPEM
X89432-illdelta SVMENRW-----LDASLSPHYLGVOGCSO
Q14628 DVPF-----IEPHALFLGIHGGKM
illbeta-1DNA CIEPNRG-----LARTKVPYFLGIQGGSR
G512010illbeta CKEOREQKSLVLDSPCVLKALHLLSQEMSEREVVFCMSFVQGEERDNKIPVALGIRDKNL

X86458spoil1  CLYCEKVGEOPTLQLE-----QKIMDLYGQPEPVKPELFYRAKTCRTSTLESVAEPD
X86459spoil2  CLYCEKVGEOPTLQLE-----QKIMDLYGQPEPVKPELFYRAKTCRTSTLESVAEPD
X89432-illdelta CLSCG-VGOEPTLILEP-----VNIMELYLGAKESKSTFYRRDMCLTSSPESAAWPG
Q14628 CLSCVKSCDETRLOLEA-----VNITDLSENKQDKRAFTIRSDSCPTLTPESAAWPG
illbeta-1DNA CLACVETECPGLQLEPSTLPPQDVNIEELYKGGCEATRTFTFOSSSCSAFRLAAAWPG
G512010illbeta YLSCVKKCEIPTLQLEE-----VDPKVMPKRNMEKREVFYKTEIKNIVEFESVLPN

X86458spoil1  WFTASS-KRDOPHILTSLELCKS----YNIAEELNIND- (SEQ ID NO: 59)
X86459spoil2  WFTASS-KRDOPHILTSLELCKS----YNIAEELNIND- (SEQ ID NO: 60)
X89432-illdelta WFLCTVPEADOPVRLTQLPENGGWNAPIIDFYFQCD- (SEQ ID NO: 61)
Q14628 WFLCTAMEADOPVSLTNMPDEG---VMVTKFYFQDE- (SEQ ID NO: 62)
illbeta-1DNA WFLCGPAEPOOPVQLTKSEPS----ARIKIFYEQSW- (SEQ ID NO: 63)
G512010illbeta WFTSTSQIEKPVFLGRFRGQ----DIIDERMETLSP (SEQ ID NO: 64)
```

Fig. 11

09730617-070901



NOVINTRA B cDNA sequence:

Regions 116968 to 117028 (1-61bp), 104067 to 104164 (62-159bp), 101958 to 102098 (160-300bp), and 100915 to 101134 (301-520bp) of genomic clone (-frame).

**ATGGGCACACCTGGCCTGGCCCTGCATGCAGACTGGACGGTGAGCCAGGACTTCTG
CAGGACACCCAAATCCTATGCTATTCGTGATTCTCGACAGATGGTGTGGGTCCTGAG
TGGAATTCTTTAATAGCAGCTCCTCTTAGCCGCAGCATTAAAGCCTGTCACCTCTTCAT
TTAATAGCCTGTAGAGACACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTA
CCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC
TACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC
AGAAGCCCTTTCTCTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTTTTCAGTCAGT
CTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAGGACAGCCCATCTTTCTC
ACCAAGGAGAGAGGCATAACTAATAACACTAACTTCTACTTAGATTCTGTGGAATA
AATCCAGC (SEQ ID NO: 9)**

Fig. 12A

NOVINTRA B Protein sequence:

**MGTPGLALHADWTVSQDFCRTPKSYAIRDSRQMVVLSGNSLIAAPLSRSIKPVTLHLI
ACRDTEFSDKEKGNMVYLGIGKDLCLFCAEIQKPTLQLKEKNIMDLIVEKKAQKPFL
FFHNKEGSTSVFQSVSPGWFIATSTTSGQPIFLTKERGITNNTNFYLDSE (SEQ ID NO: 10)**

Fig. 12B

0973067-070901



BlastN for NOVINTRA B:

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Plus Strand_HSPs:

Score = 309 (46.4 bits), Expect = 1.1e-07, P = 1.1e-07

Identities = 197/331 (59%), Positives = 197/331 (59%), Strand = Plus / Plus

Query: 169 CATTTAATAGCCTGTA-GAGAC-ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTT 226
CA TA TA CTG A GAGA A AGA T GTG C G AG T AT T GT T

Sbjct: 217 CAAATACTAACTGGAAGAGAAGATAGATGTG-GTGCCT--GTTGAGCCTCATTTTGTGT 273

Query: 227 ACCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC-T 285
CCTGGG ATC A GGA A CT TG CT T CTGTG AA T C GG A G T

Sbjct: 274 TCCTGGGGATCCATGGAGGGAAGCTGTGCCTGTCTGTGTC-AAGT-CTGGTGATGAGAT 331

Query: 286 -ACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC-AGA 343
A T CAG T A G A AA ATCA GACCTG A GA AG AGCA A A

Sbjct: 332 GAAGCTCCAGTTGGACGCAGTTAACATCACAGACCTG-AGAAAGAACAGCGAGCAGGACA 390

Query: 344 AGCCCTTTCTCTTTTTCCACAATAA-AGAAGGCTCCACTTCTGTCTTTTCAGTCAGTCTCT 402
AGC CTT CTT TCC C A AG GGC CCAC C CTTT AGTCAG C C

Sbjct: 391 AGCGCTTCACCTTCATCCGCTCCGACAGT-GGCCCCACCACCAGCTTTGAGTCAGCCGCC 449

Query: 403 TACCCTGGCTGGTTCATAGCCACCTCCACCACAT-CAGGACAGCCCATCTTTCTCACCAA 461
T CCTGGCTGGTTC T CAC T CAC A A CAG CAGCC T CTCACCAA

Sbjct: 450 TGTCTGGCTGGTTCCTCTGCAC-TGCACTAGAGGCAGACCAGCCTGTTGGCCTCACCAA 508

Query: 462 GGAGAG-AG-GCATAACT-AATAACACTAACTTCTACTT 497 (SEQ ID NO: 65)

G A GCA T AA CAC AA TTCTACTT (SEQ ID NO: 66)

Sbjct: 509 CACGCCCAAAGCAGCCGTCAAGGTCACCAAGTTCTACTT 547 (SEQ ID NO: 67)

Fig. 13A

05/30/97 07:05:01



BlastX for NOVINTRA B:

>ptnr:SPTREMBL-ACC:Q9UHA5 FIL1 ETA - Homo sapiens (Human), 157 aa.
Plus Strand HSPs:

Score = 777 (273.5 bits), Expect = 3.2e-76, P = 3.2e-76
Identities = 149/149 (100%), Positives = 149/149 (100%), Frame = +1

Query: 64 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLLIACRDTEFSDKEKGNMVYLGIGK 243
PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLLIACRDTEFSDKEKGNMVYLGIGK
Sbjct: 9 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLLIACRDTEFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQGKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 423
KDLCLFCAEIQGKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA
Sbjct: 69 KDLCLFCAEIQGKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 128

Query: 424 TSTTSGQPIFLTKEGKITNNTNFYLDSE 510 (SEQ ID NO: 68)
TSTTSGQPIFLTKEGKITNNTNFYLDSE (SEQ ID NO: 69)
Sbjct: 129 TSTTSGQPIFLTKEGKITNNTNFYLDSE 157 (SEQ ID NO: 70)

>ptnr:SPTREMBL-ACC:Q9NZH7 INTERLEUKIN-1 HOMOLOG 2 - Homo sapiens (Human), 164 aa.
Plus Strand HSPs:

Score = 411 (144.7 bits), Expect = 1.9e-37, P = 1.9e-37
Identities = 80/85 (94%), Positives = 81/85 (95%), Frame = +1

Query: 64 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLLIACRDTEFSDKEKGNMVYLGIGK 243
PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLLIACRDTEFSDKEKGNMVYLGIGK
Sbjct: 9 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLLIACRDTEFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQGKPTLQLKEKNIMD 318 (SEQ ID NO: 71)
KDLCLFCAEIQGKPTLQLK + D (SEQ ID NO: 72)
Sbjct: 69 KDLCLFCAEIQGKPTLQLKLQGSQD 93 (SEQ ID NO: 73)

>ptnr:TREMBLNEW-ACC:AAF02757 INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG
- Homo sapiens (Human), 155 aa.

Top Previous Match Next Match
Plus Strand HSPs:

Score = 197 (69.3 bits), Expect = 5.9e-15, P = 5.9e-15
Identities = 52/147 (35%), Positives = 76/147 (51%), Frame = +1

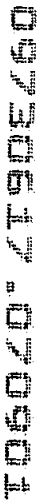
Query: 73 YAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLLIACRDTEFSDKEKGNMVYLGIGK 252
+ ++DS V L N L+A L K + I+ + D ++ LG++G
Sbjct: 9 FRMKDSALKVLYLHNNQLLAGGLHAG-KVIKGEEISVVPNRWLDASLSPVI-LGVQGSQ 66

Query: 253 CLFCAEIQGKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIATST 432
CL C Q +PTL L+ NIM+LY+ K K F F+ G TS F+S +YPGWF+ T
Sbjct: 67 CLSCGVGQ-EPTLTLEPVNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGWFLCTVP 125

Query: 433 TSGQPIFLTK--ERGITNN--TNFYLDSE 510 (SEQ ID NO: 74)
+ QP+ LT+ E G N T+FY + (SEQ ID NO: 75)
Sbjct: 126 EADQPVRLTQLPENGWNAPITDFYFQQCD 155 (SEQ ID NO: 76)

Fig. 13B

09730617.070901



Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

2) X86459spoII2 (cDNA encoding a human spoII-II protein; Q14628 (intracellular IL-1 receptor antagonist type II-human); AAF02757 (intracellular IL-1 receptor antagonist type II-human); G512010; (OVINE IL-1 BETA - Pig)

```

illbeta2DNA      -----MCPGLALHADWTVS-----
X86459spoil2     -----DNHMTMRCPDADGGGRAVYCSSES-----
Q14628           -----MALADLYEECGGGGGEGEDNADSKE-----
AAF02757         -----
G51201oillbeta  MATVPEPINEVMAYYSDENELLFEVDGPKOMKSCTOHLDLCSMGDGNIOLOISHLYNKS

```

```

i11beta2DNA      -----FCRT-----PKSYAIR-----
X86459spoil2     AVGMGLWRLRPSALTLSPEVAPAFSAPLCTLPFPVCK-PTGTGIN-
Q14628           -----TICRPSGRKSSK-MQAFRIW-----
AAF02757         -----MVLSG-ALCFRMK-----
G512010i11beta   FROVVSVIVAMEKLRSRAYEHVFRDDDLRSILSFIFEEEPVIFETSSDELLCDAAVOSVK

```

```

illbeta2DNA      ----DSROMVIVLSSNSLIARPLSRSIKPVILHLIAACRDTEFSDK-EKGNMVLGLIKCKD
X86459spoil2     ----DLNQCVITLQGNLVAVPRSDSVTPVAVAVITCKYPEALEQ-GRGDPVILGIONPE
Q14628           ----DVNKTLYLRNLSLVAGYLO-GPNVNLEEKIDVVP-----IEPHAVILGHICGK
AAF02757         ----DSNKKVLYLHNNLLAGLGH-AGKVIKGEELSVVNRNRLD-ASLSPVILGVQGS
G512010illbeta   CKLODREQSLVLDS-PCVLKALHLLSQEMSREVFQMSFVQGEERDNKIPVALGRDKN

```

illbeta2DNA
 X86459spoil2
 Q14628
 AAF02757
 G512010illbeta

```

illbeta2DNA      TTSCOPFIFLTKER--C--ITNNTNFYLDSE- (SEQ ID NO: 77)
X86459spoil2    KRD-OPHILTSEL--C--KSYNTAFELNIND- (SEQ ID NO: 78)
Q14628          MEADQPVSLTNMPDEC--VMVFKEYFQDEE- (SEQ ID NO: 79)
AAF02757        PEADQPVRLTQLPENGWGNAPITDFYQQCD- (SEQ ID NO: 80)
G512010illbeta  QIEKPVFLGRFR--C--GQDIDFRMETLSP (SEQ ID NO: 81)

```

Fig. 14



NOVINTRA C cDNA sequence:

Region 168700 to 168880 (1-181bp), 169967 to 170118 (182-331bp) and 170635 to 170694 332-391bp) of the genomic clone (- frame).

GATATCAATCATCGGGTGTGGGTCTTCAGGACCAGACGCTCATAGCAGTCCCGAGG
AAGGTGTTCCAGTCACTATTGCCTTAATCTCATGCCGACATGTGGAGACCCTTGAG
AAAGACAGAGGGAACCCCATCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGAT
GTGTGCTAAAGTCGGGGACCAGCCACACTGCAGCTGAAGCTTCAGGAAAAGGATA
TAATGGATTTGTACAACCAACCCGAGCCTGTGAAGTCCTTTCTCTTCTACCACAGCC
AGAGTGGCAGGAACCTCCACCTTCGAGTCTGTGGCTTTCCCTGGCTGGTTCATCGCTG
TCAGCTCTGAAGGAGGCTGTCCTCTCATCCTTACCCAAGAACTGGGGAAAG (SEQ ID NO: 11)

Fig. 15A

NOVINTRA C Protein sequence:

DINHRVWVLQDQTLIAVPRKVPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCIMCAK
VGDQPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIAVSSEGGC
PLILTQELGK (SEQ ID NO: 12)

Fig. 15B

BlastN for NOVINTRA C:

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Minus Strand-HSPs:

Score = 274 (41.1 bits), Expect = 5.6e-06, P = 5.6e-06
Identities = 150/244 (61%), Positives = 150/244 (61%), Strand = Minus / Plus

Query: 258 TCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGATGTGTGCTAAAGTCGGG-GACCAG 200
T T CCTGGG T ATGGA AA CT TGCCTG TGTG T AAGTC GG GA AG
Sbjct: 271 TGTTCCTGGGGATCCATGGAGGAAGCTGTGCCTGTCTCTGTG-TCAAGTCTGGTGATGAG 329
Query: 199 CCCACACTGCAGCTGAAGCTTCAGGAAAAGGATATAATGGATTTGTACAACCAACC-CGA 141
A CT CAG TG A C CAG AA AT A GA TG A AA AAC CGA
Sbjct: 330 ATGAAGCTCCAGTTGGA-CG-CAGTTAAC----ATCACAGACCTG-AGAAAGAACAGCGA 382
Query: 140 GCCTGTGAAGTCCTTTCTCTTCTACCACAGCCAGAGTGGCAGGAACCTCCACCTTCGAGTC 81
GC G AAG CTT CTTC CC C C A AGTGGC A C CCA CTT GAGTC
Sbjct: 383 GCAGGACAAGCGCTTCACCTTCATCCGCTCCGACAGTGGCCCCACCACCAGCTTTGAGTC 442
Query: 80 TGTGGCTTTCCCTGGCTGGTTCATCGCTGT-CAGCTCTGAAGG-AGGCTGTCCTCTCATC 23
G GC T CCTGGCTGGTTC TC TG C GC CT AGG AG C CCT T C
Sbjct: 443 AGCCGCCTGTCTCTGGCTGGTTCCTC--TGCAGTGCAGTAGAGGCAGACCAGCCTGTTGGC 500
Query: 22 CTTACCCA 15 (SEQ ID NO: 82)
CT ACC A (SEQ ID NO: 83)
Sbjct: 501 CTCACCAA 508 (SEQ ID NO: 84)

Fig. 16A

1050/0/1990/60



BlastX for NOVINTRA C:

>ptnr:SPTREMBL-ACC:Q9UHA7 FIL1 EPSILON - Homo sapiens (Human), 158 aa.
Plus Strand HSPs:

Score = 646 (227.4 bits), Expect = 2.4e-62, P = 2.4e-62
Identities = 126/130 (96%), Positives = 127/130 (97%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYLGNGNLNLCMC 174
DINHRVWVLQDQTLIAVPRK + PVTIALISCRHVETLEKDRGNPIYLGNGNLNLCMC
Sbjct: 17 DINHRVWVLQDQTLIAVPRKDRMSPVTIALISCRHVETLEKDRGNPIYLGNGNLNLCMC 76

Query: 175 AKVGDQPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 354
AKVGDQPTLQLK EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG
Sbjct: 77 AKVGDQPTLQLK--EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 134

Query: 355 GCPLILTQELGK 390 (SEQ ID NO: 85)
GCPLILTQELGK (SEQ ID NO: 86)
Sbjct: 135 GCPLILTQELGK 146 (SEQ ID NO: 87)

>ptnr:SPTREMBL-ACC:Q9NZH8 INTERLEUKIN-1 HOMOLOG 1 - Homo sapiens, 169 aa.

Plus Strand HSPs:

Score = 416 (146.4 bits), Expect = 5.7e-38, P = 5.7e-38
Identities = 82/130 (63%), Positives = 101/130 (77%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYLGNGNLNLCMC 174
D+N +VW LQ Q L+AVPR V PVT+A+I+C++ E LE+ RG+PIYLG+ +CL C
Sbjct: 29 DLNQQVWTLQGNLVAVPRSDSVTPVTAVITCKYPEALEQGRGDPYILGIQNPEMCLYC 88

Query: 175 AKVGDQPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 354
KVG+QPTLQLK E+ IMDLY QPEPVK FLFY +++GR ST ESVAFP WFIA SS+
Sbjct: 89 EKVGQPTLQLK--EQKIMDLYGQPEPVKPFIFYRAKTGRTSTLESVAFPDWFIA-SSKR 145

Query: 355 GCPLILTQELGK 390 (SEQ ID NO: 88)
P+ILT ELGK (SEQ ID NO: 89)
Sbjct: 146 DQPIILTSELGK 157 (SEQ ID NO: 90)

>ptnr:SWISSPROT-ACC:P25085 INTERLEUKIN-1 RECEPTOR ANTAGONIST PROTEIN
PRECURSOR (IL-1RA) (IL-1RN) (IRAP) - Mus musculus (Mouse), 178 aa.

Top Previous Match Next Match

Minus Strand HSPs:

Score = 173 (60.9 bits), Expect = 2.1e-12, P = 2.1e-12
Identities = 35/81 (43%), Positives = 50/81 (61%), Frame = -1

Query: 259 IYLGNGNLNLCMCAKVGDPPTLQLKLQEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFES 80
++LG++G LCL CAK GD ++L+L+E +I DL E K F F S+ G ++FES
Sbjct: 82 VFLGIHGKLCCLSCAKSGDD--IKLQLEEVNITDLSKNKEEDKRFTFIRSEKGPPTS FES 139

Query: 79 VAFPGWFIASSEGCGPLILT 17 (SEQ ID NO: 91)
A PGWF+ + E P+ LT (SEQ ID NO: 92)
Sbjct: 140 AACPGWFLCTTLEADRPVSLT 160 (SEQ ID NO: 93)

Fig. 16B

1060707196617-070901



ClustalW for NOVINTRA C:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) IL1X_MOUSE: Locus - IL1X_MOUSE; Accession - P25085; PID - g124313
- 2) IL1X_HORSE: Locus - IL1X_HORSE; Accession - 018999; PID - g6166230
- 3) AAF02757_HUMAN: Locus - AF186094_1; Accession - AAF02757; PID - g6049805

IL1X_MOUSE	MEICWGPYSHLISLLILLEHSEAACRPSGKRPCCKMQAFRIWDINOKIFYLRRNNQLIAGY
IL1X_HORSE	MEIRRRRSVRHLIS-LLLFLEHYSETACHPLGKRPCCKMQAFRIWDVNOKIFYMRNNQLVAGY
AAF02757 Human	-----MVLSCALC-----FRMKDSALKVLYLHNNQLIAGG
Novel_IL1	-----DINHRVWVLODOTLIAMP

IL1X_MOUSE	LOGPNIKLE----EKIDMVP-----TELHSVFLGIHGGKLCCLSCAKSCDEIKLOLEEVN-
IL1X_HORSE	LCESNTKLO----EKIDVVP-----LEPDALFLGLHGRKLCACVKSDEIRFOLEAVN-
AAF02757 Human	LHAGKVIKG----EELSVVENRWLDASLSPVILGVCGGSQCLSCG-VGQEPFLILEPVN-
Novel_IL1	RKVFPVTEHALISCRHVETLEK----DRGNPIYLGINCLNLCIMCAKVGDPQLQLKLEK

IL1X_MOUSE	-ITDLSKNKEEDKRFTFIRSEKGPISFESAACPGWFLCTLEADRPVSLTNIPEE---P
IL1X_HORSE	-ITDLSKNKEENKRFTFIRNSGPTISFESAACPGWFLCTAQEADRPVSLTNKPKE---S
AAF02757 Human	-IMELYLGAKESKSTTFYRRDMGLISFESAAYPGWFLCTVPEADCPVRLTQLPENGAWN
Novel_IL1	DIMDLYNQPEPVKSELFYHSQSGRNSIFESVAFPGWFIIVSSEEGCPILTLSELGK----

IL1X_MOUSE	LEVTKFYFOEDQ (SEQ ID NO: 94)
IL1X_HORSE	FEVTKFYLOEDQ (SEQ ID NO: 95)
AAF02757 Human	AFETDFYFOQCD (SEQ ID NO: 96)
Novel_IL1	----- (SEQ ID NO: 97)

Fig. 17

09730617.070901

05730617-070501
105020-1905/60

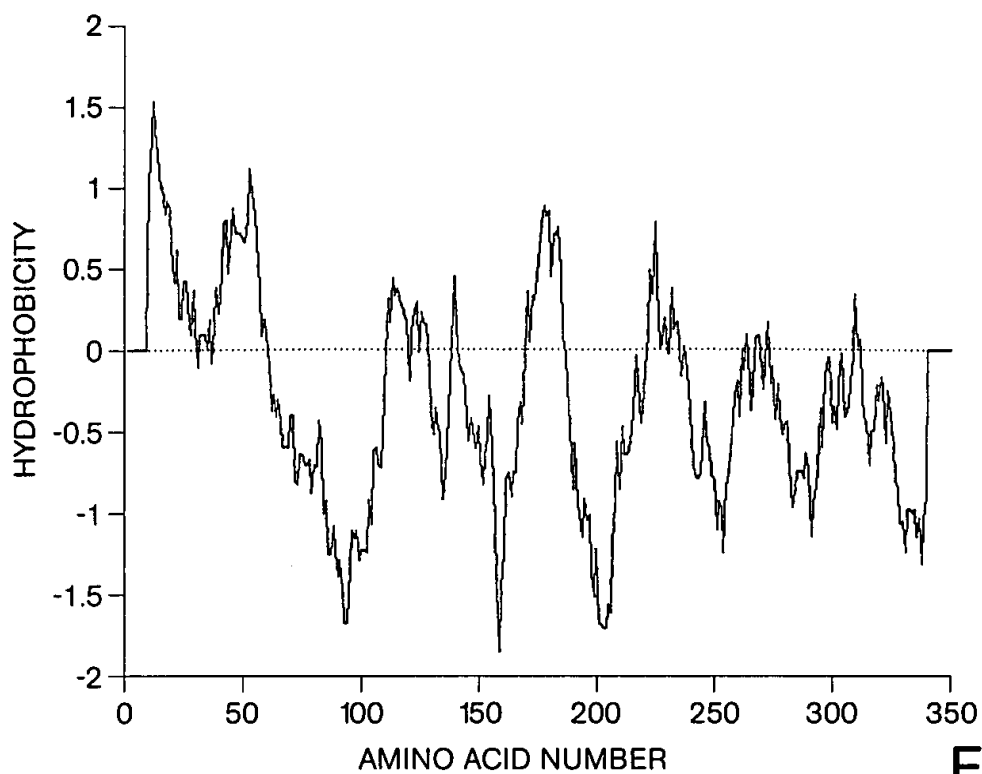


Fig. 18

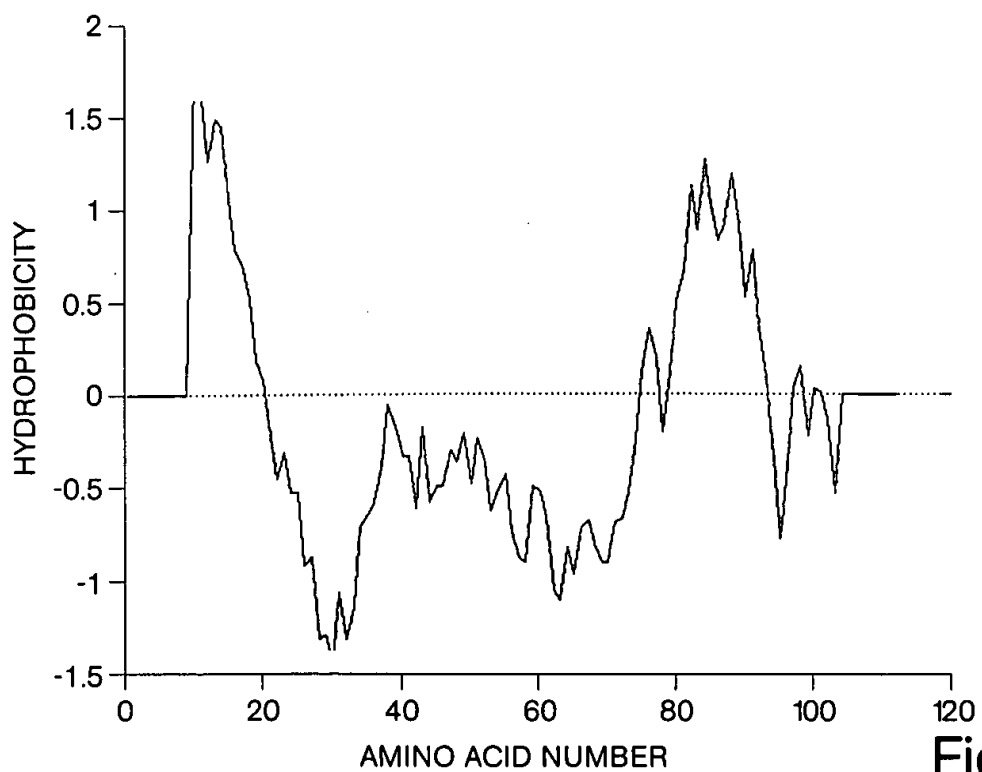


Fig. 19

09750617 078901
105070 71905750

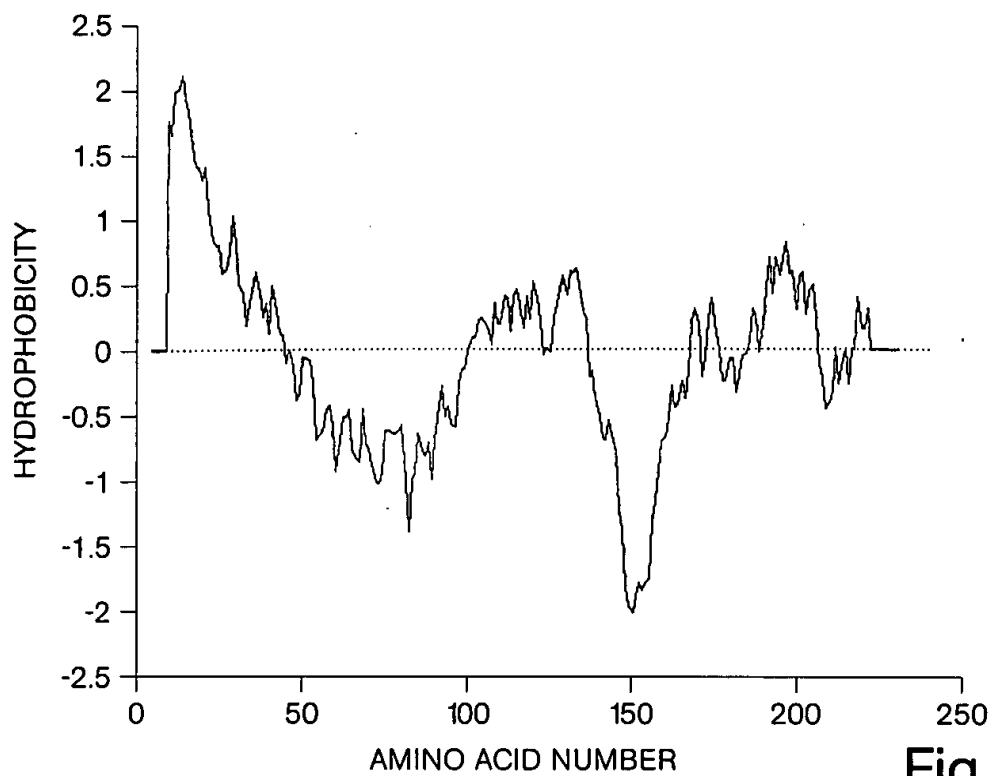


Fig. 20

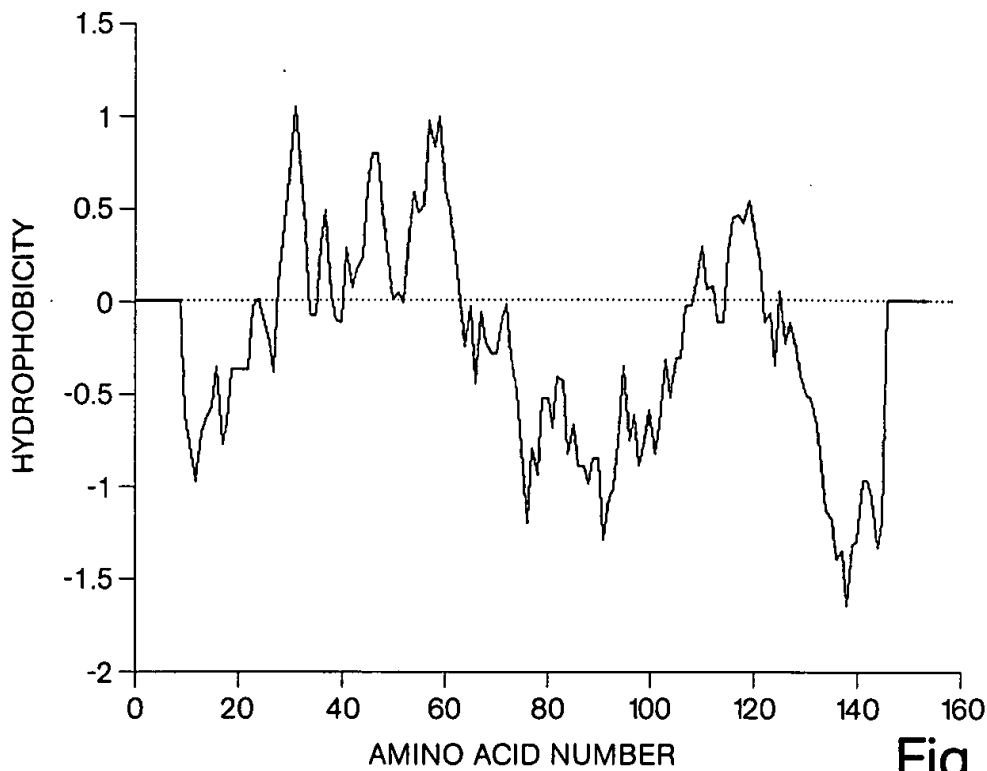


Fig. 21

FD5070-7905750

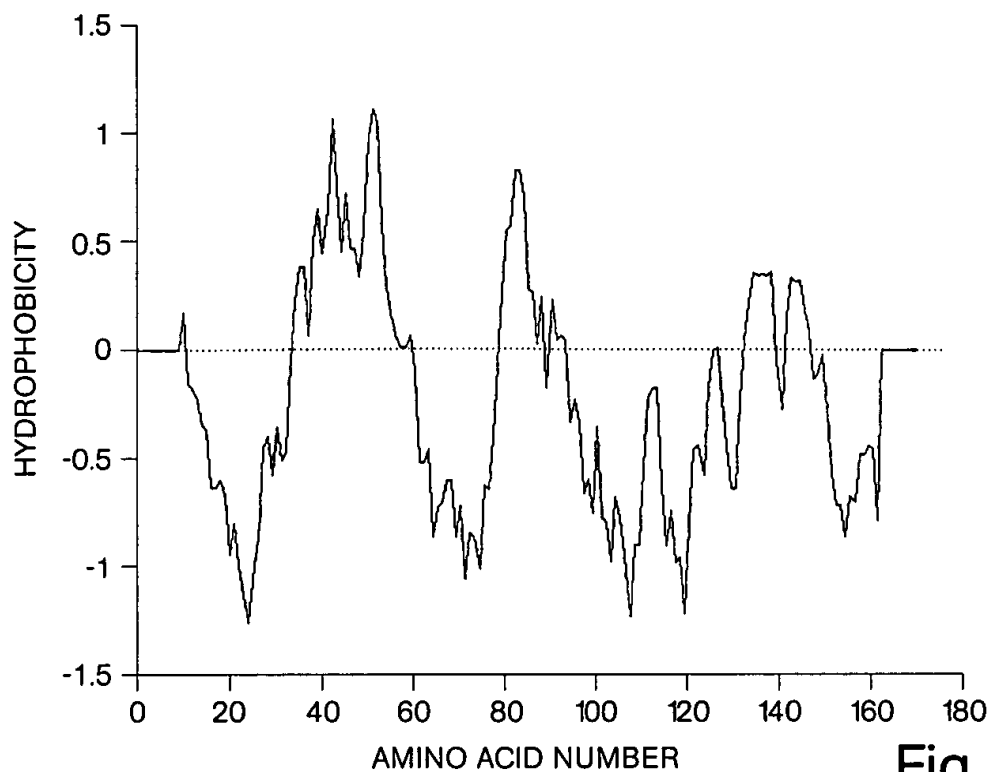


Fig. 22

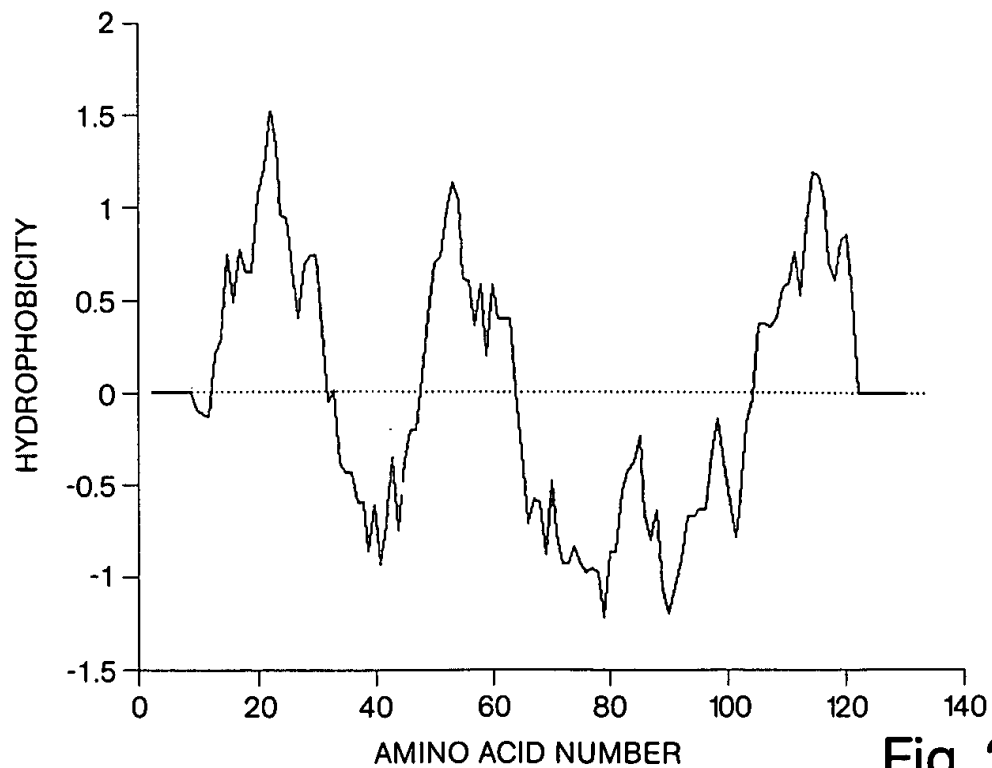


Fig. 23